REMARKS/ARGUMENTS

Reconsideration in view of the remarks and arguments which follow is respectfully requested.

Status of the Claims

Claims 1, 3, 4, 9, 10, 20, 22, 23, 28, 45, and 46 are undergoing examination, and have been rejected as discussed in the following comments. Claims 1, 9, 20, and, 28 have been amended and claims 51-55 have been added. Claims 11-13, 15-19, 29-31, 33-37, and 40 were previously withdrawn.

Amendments

The specification has been amended to a minor error, the correction of which would have been obvious to a skilled worker. *See* MPEP § 2163.07 II, Obvious Errors. The specification has been amended on page 8 at ¶56 of the '807 Publication to state "*Salmonella typhi*" rather than "*Shigella*". A skilled worker would have readily recognized that the reference to *Shigella* was an obvious error, and should have referred to "*Salmonella typhi*" as the strain to which Ty21a belongs because Ty21a is a specific *Salmonella typhi* strain, not a Shigella strain. Support for this amendment may be found, for example, in Pasetti et al., *Clin. Immunol.*, 1999, 92:76-89 (copy enclosed; *See* Tab A, page 86, the middle of column 1 stating "Fennelly and colleagues have recently reported that attenuated *S.typhi* vaccine strain Ty21a harboring a eukaryotic expression plasmid encoding antigens of measles virus was able to induce cytotoxic responses against the foreign antigens when given intraperitoneally to Balb/c mice."). Additionally, Applicants direct the Examiner to Murphy et al., *Infection and Immunity, 1991*, 59(11): 4291-4293 that is entitled "Immunogenicity of *Salmonella typhi* Ty21a Vaccine for Young Children" (copy enclosed; *See* Tab B). Thus, it is clear from both Pasetti et al. (1999) and Murphy et al. (1991) that Ty21a belongs to the *Salmonella typhi* strain, not the a *Shigella* strain, and that a skilled worker would have readily recognized reference of Ty21a as belonging to a *Shigella* strain as a minor error and *Samonella typhi* as the correction of this minor error. Accordingly, Applicants respectfully request

consideration of and entry of the amendment to the specification to correct the minor error. No new matter has been added.

Claim 1 has been amended to recite "consisting essentially of" rather than "comprising". Claims 1 and 9 have been amended to recite "consisting of one of an adjuvant and a delivery vehicle" rather than "antigen carrier or delivery vehicle". Support for this amendment may be found, for example, in U.S. Patent Application Publication No. 2007/0059807 (hereafter "the '807 Publication") which is the publication of the application as filed, on page 2, ¶15 and on page 4 ¶27. Claims 1 and 20 have been amended to delete the phrase "the composition is suitable for mucosal administration", and to delete the word "predominantly", and to specify that the mammalian prion protein is non-amyloidogenic. Support for this amendment may be found, for example, in the '807 Publication on page 4, ¶33. Claim 20 has also been amended to recite "an attenuated bacterium microorganism consisting of one of a *Shigella* strain and a *Salmonella* strain" rather than "an attenuated *Salmonella typhii* bacterium transfected spp strain. Support for this amendment may be found, for example, in the '807 Publication on page 4, ¶27 and ¶56.

New claim 51 depends from claim 20 and recites that the attenuated bacterium microorganism is a *Salmonella* bacterium transfected spp strain. Support for this claim may be found, for example, in the '807 Publication on page 4, ¶19. Claim 28 has been amended to depend from new claim 51 rather than claim 20. Support for this claim may be found, for example, in the '807 Publication on page 4, ¶27. Claim 28 has also been amended to delete reference to LVR03 and to *Salmonella typhi* CVD915, and to add reference to *Salmonella typhi* Ty21a. Support for reference to *Salmonella typhi* Ty21a is found in the application as filed as discussed in the foregoing comments. New claim 52 depends from claim 20 and recites that the attenuated bacterium microorganism is a *Shigella* strain. Support for this claim may be found, for example, in the '807 Publication on page 4, ¶27 and ¶56. New claim 53 depends from claims 3, 22, and 45, and recites that at least one amino acid residue is a D-amino acid residue. Support for this claim may be found, for example, in the '807 Publication on page 2, ¶15.

New claim 54 is an independent claim directed to a composition consisting essentially of an isolated non-amyloidogenic noninfectious mammalian prion protein and consisting of one of an adjuvant and delivery vehicle wherein the isolated mammalian prion protein is selected from the group consisting of bovine, deer, elk, and sheep prion protein; and the composition elicits a humoral immune response that is associated with a mucosal IgA response and any concomitant immunoglobulin counterpart in other bodily fluids when introduced to a mammalian mucosal immune system. New claim 55 is an independent claim directed to a composition comprising an attenuated bacterium microorganism consisting of one of a *Shigella* strain and a *Salmonella* strain transformed with a vector capable of expressing an isolated non-amyloidogenic mammalian prion protein, wherein the isolated mammalian prion protein is selected from the group consisting of bovine, deer, elk, and sheep prion protein; and the composition elicits a humoral immune response that is associated with an IgA response and any concomitant immunoglobulin counterpart in other bodily fluids when introduced to a mammalian mucosal immune system. Support for claims 54 and 55 may be found throughout the application as filed; for example, in the '807 Publication on page 1, ¶8, the Abstract on the cover of the '807 Publication, and page 3, ¶26 to page 4, ¶28.

No new matter has been added. Applicants expressly reserve the right to pursue any cancelled subject matter in subsequent applications that claim benefit from this application. Entry of the amendments and reconsideration of the pending claims is respectfully requested.

Rejection Under 35 U.S.C. § 112, First Paragraph ("Written Description")

Claim 28 continues to be rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. The Examiner previously noted that amended claim 28 requires *Salmonella typhimurium* LVR01 and SL3261 and *Salmonella enteritidis* LVR02, which must be obtainable by a repeatable method set forth in the application or otherwise readily available to the public.

Applicants appreciate the Examiner's acknowledgement of the request made in the Amendment dated January 15, 2009 that this rejection be held in abeyance until one or more claims

are found to be allowable at which time, we will make and/or document an acceptable deposit of the biological organisms encompassed by the allowed claim(s).

Rejections Under 35 U.S.C. § 103(a)

The Examiner is thanked for notifying Applicants that the following previous obviousness rejections have been withdrawn: (1) claim 3 over U.S. Patent Application Publication No. 2003/0219459 to Bachmann et al. (hereafter "Bachmann") in view of U.S. Patent No. 6,514,503 to Gizurarson et al. ("Gizurarson") and (2) claim 45 over Bachmann, Gizurarson, and U.S. Patent No. 5,733,760 (hereafter "Lu") in view of Chabalgoity et al. (*Vaccine*, 2001, Vol. 19, p. 460-469; hereafter "Chabalgoity")).

As discussed in the following comments, the Examiner has maintained her rejections of claims 1, 4, 9, 10, 20, 22, 23, 28, and 46, and has issued new reasons for why claims 3 and 45 are obvious over a combination of previously and newly cited prior art.

Claims 1 and 9

The Examiner has maintained her rejection of independent claim 1 and claim 9 that depends from it under 35 U.S.C. § 103(a) as obvious over Bachmann in view of Gizurarson.

According to the Examiner, Bachmann discloses prion-protein conjugates, including mammalian prions such as mouse, human, deer, and elk (*see* Bachmann, claims 14 and 15). The Examiner also states that Bachmann discloses aluminum hydroxide as an adjuvant (*see, e.g.*, ¶ 80). The Examiner acknowledges that Bachmann does not teach a composition suitable for mucosal administration. For this, the Examiner relies upon Gizurarson as disclosing compositions suitable for mucosal administration. The Examiner maintains her reasons in the Office Action dated August 7, 2008 for why the pending claims are obvious over Bachmann in view of Gizurarson. According to the Examiner it would have been obvious for a skilled worker to provide the composition taught by Bachmann comprising prion proteins for mucosal administration as taught by Gizurarson. *See*,

Office Action dated August 7, 2008, pages 4-6. Unconvinced by our arguments in the previous response, the Examiner states that Bachmann's composition requiring an isolated prion protein and alum in a virus-like protein anticipates the composition of the instant claims. *See*, Office Action dated March 31, 2009, page 5. This rejection is respectfully traversed.

Amended claim 1 calls for a composition consisting essentially of an isolated non-amyloidogenic mammalian prion protein and consisting of one of an adjuvant and a delivery vehicle, wherein the isolated mammalian prion protein is selected from the group consisting of bovine, deer, elk, and sheep prion protein; and the composition elicits a humoral immune response that is associated with a mucosal IgA response and any concomitant immunoglobulin counterpart in other bodily fluids when introduced to a mammalian mucosal immune system. Amended claim 9 specifies that the adjuvant is cholera toxin subunit B (CT-B) or heat-labile enterotoxin (LT) and the delivery vehicle is aluminum hydroxide. *No combination of the cited references teaches or suggests the combination of uses and features, called for in the pending claims.*

A skilled worker having read Bachmann would not have been led to arrive at the current claims because Bachmann teaches a composition comprising an isolated protein, alum, and a virus-like protein (hereafter "VLP"). The amended claims do not require a VLP. The VLP of the Bachmann composition is a critical element that improves the efficiency of vaccination by increasing the degree of repetitiveness of the antigen. *See*, Bachmann, paragraph [0012]. Furthermore, Bachmann discusses that a VLP is a core particle having a structure with an inherent organization that is bound to prion protein, dimers thereof, or prion peptides. *See*, Bachmann, paragraph [0014]. Additionally, Bachmann discloses that a prior protein is an antigen or antigenic determinant that interacts with a VLP to form an ordered and repetitive antigen array. *See*, Bachmann, paragraph [0015].

As used in the Bachmann composition, the function of a VLP is to elicit an immune response because the VLP mimics the structure of an authentic virus particle, and is readily recognized by the immune system. Additionally, a VLP ensures presentation of a viral antigen in a more authentic confirmation than if the VLP was not used. A skilled worker having read Bachmann

would have recognized that recombinant proteins when used as an antigen may be poor immunogens because of incorrect folding of the protein or poor presentation to the immune system. In fact, the same skilled worker after reading Bachmann would not have had an expectation of success to arrive at the compositions as required by the pending claims because he would have thought that a VLP is necessary to use a recombinant protein as an immunogen.

A skilled worker would not have looked to Bachmann to arrive upon the pending claims because Bachmann teaches that an isolated prion protein is not efficient at eliciting an immune response. A skilled worker would not have had a reasonable expectation of success to elicit an immune response using a composition that did not include a VLP.

Furthermore, a skilled worker would not have looked to the teachings of Gizurarson to arrive at the invention as called for by the pending claims. Gizurarson discloses mucosal delivery of compositions comprising a glyceride and a non-self (*i.e.*, foreign) antigen. The Examiner states that Gizurarson "provides a motivation to use mucosal administration of ***pathogenic*** antigens". *See*, Office Action dated March 31, 2009; emphasis added. Also in the current Office Action, the Examiner incorrectly characterizes the current invention by noting "that the pathogenic form of prion protein is not considered a self antigen and therefore it would have been expected that when administered mucosally it would induce immune responses against the prion protein as suggested by Gizurarson." *See*, March 31, 2009 Office Action, page 6. Applicants respectfully disagree with the Examiner's statements as they concern the claimed invention. The current invention as called for by the amended claims does not require a pathogenic prion protein. Instead, the amended claims require an isolated non-amyloidogenic mammalian prion protein (*i.e.*, non-pathogenic prion protein). Thus, Gizurarson, for the reasons that the Examiner relies upon it, is not applicable to the current invention as called for by the amended claims because it does not teach or suggest mucosal delivery of a self-antigen.

Furthermore, Applicants, in the Amendment dated January 15, 2009, had directed the Examiner to Czerkinsky *et al.*, (*Immunological Reviews* 170:197-222 (1999); hereafter "Czerkinsky") as teaching that it was well accepted in the art, at the time of filing of the application,

that mucosal administration of a self-antigen would lead to immune tolerance. *See*, Amendment dated January 15, 2009, pages 10-11. However, as discussed in the foregoing comments, the Examiner did not fully appreciate Applicants' reasons for pointing to Czerkinsky because the Examiner did not appreciate that the pending claims call for a self-antigen, not a pathogenic prion protein.

Moreover, as discussed in greater detail in Applicants' Amendment dated January 15, 2009, a skilled worker familiar with Gizurarson would also have been familiar with Czerkinsky; and, thus, the skilled worker would not have had a reasonable expectation of success for making a composition consisting essentially of an isolated non-amyloidogenic mammalian prion protein and consisting of one of an adjuvant and a delivery vehicle to elicit a humoral immune response that is associated with a mucosal IgA response with a composition containing a self-antigen. Instead, the same skilled worker would have expected that administration of a self-antigen would have resulted in immune tolerance. This would defeat the purpose of the claimed composition.

The differences between the prior art and the pending claims are significant because the prior art provides no guidance or reasonable expectation of success for preparing or using the composition as called for by the present claims; and the level of ordinary skill in this art is relatively high. *See KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1734 (2007); *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 15-17 (1966).

As discussed in the foregoing comments, reasons are provided why one of ordinary skill in the art, even if so motivated, would not have had a reasonable expectation of success to combine the claimed elements to successfully arrive upon the compositions as claimed. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990). In fact, in this case, Bachmann teaches that a VLP is necessary in order to use a recombinant protein as an immunogen. Additionally, Gizurarson teaches use of a foreign antigen, not a self-antigen as is required by the amended claims. In other words, the cited prior art documents do not teach, let alone suggest, the desirability of combining the documents.

Furthermore, Czerkinsky, as discussed in the foregoing comments, would not have led a skilled worker to prepare the claimed compositions. The particular features of the claimed compositions, as described in the foregoing comments, establish that it would not have been within the technical grasp of a skilled worker to have had a reasonable expectation of success for making or using the claimed compositions by combining discrete elements of the cited prior art, alone, or in combination with one another because at the time of filing of the current application it was thought that mucosal administration of a self-antigen would lead to immune tolerance.

In fact, it was only through experiments carried out by the present inventors as described in the specification that the parameters for the inventive compositions were determined and tested, and shown to elicit a humoral immune response that is associated with a mucosal IgA response and any concomitant immunoglobulin counterpart in other bodily fluids when introduced to a mammalian mucosal immune system. MPEP § 2145(X)(B); *In re Dow Chemical Co.*, 837 F.2d 469 (Fed. Cir. 1988).

For at least the reasons set forth above, amended claims 1 and 9 are not obvious over Bachmann in view of Gizurarson. Reconsideration of amended claims 1 and 9 and withdrawal of the rejection of these claims under 35 U.S.C. § 103(a) is respectfully requested.

New claim 54 is not obvious over Bachmann in view of Gizurarson for the same reasons as discussed in the foregoing comments because claim 54 is similar in scope to amended claim 1. New claim 54 differs from amended claim 1 by specifying an isolated non-amyloidogenic noninfectious mammalian prion protein. Thus, the arguments discussed in the foregoing comments with respect to claim 1 are also applicable to why new claim 54 is not obvious over Bachmann in view of Gizurarson.

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Claim 4

The Examiner also has maintained her rejection of claim 4 under 35 U.S.C. § 103(a) as obvious over Bachmann and Gizurarson and further in view of Benkirane et al. (*J. Biol. Chem.*,

1993, Vol. 268, p. 26279-26285; hereafter "Benkirane") for the reasons stated in the Office Action dated August 7, 2008. According to the Examiner in the Office Action dated August 7, 2008, Benkirane discloses that D-residues significantly increase the antigenicity of antigenic peptides and lead to the generation of high levels of IgG_3 antibodies. Based upon this, the Examiner concludes that it would have been obvious to a person of ordinary skill in the art to make a vaccine composition using peptides composed of D-amino acids. *See*, Office Action dated August 7, 2008, pages 6-8. This rejection is respectfully traversed.

Claim 4 depends from amended claim 1, and further specifies that the amino acid residues are D-amino acids. Thus, claim 4 is not obvious over Bachmann and Gizurarson for the reasons discussed in the foregoing comments with respect to claim 1. Benkirane does not cure the deficiency of either Bachmann and Gizurarson because Benkirane does not teach or suggest the claimed composition consisting essentially of an isolated non-amyloidogenic prion protein (*i.e.*, a self-antigen) and consisting of one of an adjuvant and a delivery vehicle to elicit a humoral immune response that is associated with a mucosal IgA response and any concomitant immunoglobulin counterpart in other bodily fluids when introduced to a mammalian mucosal immune system.

For at least the reasons set forth above, pending claim 4 is not obvious over Bachmann in and Gizurarson and further in view of Benkirane. Reconsideration of pending claim 4 and withdrawal of the rejection of this claim under 35 U.S.C. § 103(a) is respectfully requested.

* * * * *

Claims 9 and 10

The Examiner also has maintained her rejection claims 9 and 10, which both depend from claim 1, under 35 U.S.C. § 103(a) as obvious over Bachmann and Gizurarson, and further in view of U.S. Patent 6,440,423 to Clements et al. (hereafter "Clements") and U.S. Patent 6,585,975 to Kleanthous et al. ("Kleanthous") for the reasons stated in the August 7, 2008 Office Action. In the Office Action dated August 7, 2008, the Examiner asserts that Clements teaches CT-B as an effective adjuvant, and Kleanthous discloses the covalent attachment of CT-B to antigenic proteins.

The Examiner also states in the Office Action dated August 7, 2008 that Clements also discloses oral (*i.e.*, mucosal) vaccines that simulate antibody responses. *See,* Office Action dated August 7, 2008, pages 9-10. This rejection is respectfully traversed.

Claim 9 depends from claim 1, and further specifies the adjuvant. Claim 10 depends from claim 9 and specifies that the prion protein is covalently attached to the cholera toxin subunit B. Claims 9 and 10 are not obvious over Bachmann and Gizurarson, and further in view for at least the reasons discussed in the foregoing comments with respect to claim 1. Neither Clements nor Kleanthous cure the deficiency of either Bachmann or Gizurarson because neither Clements nor Kleanthous teach or suggest the claimed composition consisting essentially of an isolated non-amyloidogenic prion protein (*i.e.*, a self-antigen) and consisting of one of an adjuvant and a delivery vehicle to elicit a humoral immune response that is associated with a mucosal IgA response and any concomitant immunoglobulin counterpart in other bodily fluids when introduced to a mammalian mucosal immune system with a composition containing a self-antigen. Additionally, as stated in the Amendment dated January 15, 2009, Kleanthous only teaches eliciting a Th1 response through parenteral administration. Kleanthous neither teaches nor suggests that a Th2-mediated (*i.e.* humoral) IgA response could be elicited by the mucosal administration of the composition as called for by the pending claims. *See*, Amendment dated January 15, 2009, page 13.

For at least the reasons set forth above, amended claim 9 and pending claim 10 are not obvious over Bachmann in view of Gizurarson and further in view of Clements and Kleanthous. Reconsideration of amended claim 9 and pending claim 10 and withdrawal of the rejection of these claims under 35 U.S.C. § 103(a) is respectfully requested.

* * * * *

Claims 20, 22, and 28

The Examiner also has maintained her rejection of independent claim 20 and claims 22 and 28 that depend from claim 20 under 35 U.S.C. § 103(a) as obvious over Bachmann, Gizurarson, and Lu et al. and further in view of Chabalgoity for the reasons stated in the Office Action dated August

7, 2008. *See*, Office Action dated August 7, 2008, pages 9-12. And, according to the Examiner in the current Office Action, Lu and Chabalgoity are cited because they teach effectiveness of *Salmonella* vectors in induction of mucosal immune responses. *See*, Office Action dated March 31, 2009, page 7. This rejection is respectfully traversed.

Amended claim 20 is directed to a composition comprising an attenuated bacterium microorganism consisting of one of a *Shigella* strain and a *Salmonella* strain transformed with a vector capable of expressing an isolated non-amyloidogenic mammalian prion protein to elicit a humoral immune response that is associated with a mucosal IgA response and any concomitant immunoglobulin counterpart in other bodily fluids when introduced to a mammalian mucosal immune system. Amended claim 28 and pending claim 22 depend indirectly or directly, respectively, from amended claim 22. Amended claim 28 further specifies particular *Salmonella* spp strains and pending claim 22 further specifies particular amino acid sequences for the non-amyloidogenic prion protein.

Amended claims 20 and 28 and pending claim 22 are not obvious over Bachmann and Gizurarson for at least similar reasons, as discussed in the foregoing comments, with respect to claim 1. As discussed in the foregoing comments, the composition of amended claim 20 is not obvious over the composition disclosed by Bachmann because amended claim 20 requires a *Shigella* strain or a *Salmonella* strain that has been transformed with a vector that expresses an isolated non-amyloidogenic mammalian prion protein. Bachmann does not suggest or teach using an attenuated bacterium microorganism that has been transfected with a self-antigen to elicit a humoral immune response that is associated with a mucosal IgA response and any concomitant immunoglobulin counterpart in other bodily fluids when introduced to a mammalian mucosal immune system. Furthermore, the Examiner relies upon Gizurarson as disclosing compositions suitable for mucosal administration; however, as discussed in the foregoing comments, Gizurarson discloses mucosal delivery of a composition comprising a glyceride and a non-self (*i.e.*, foreign) antigen, and does not suggest or teach use of a self-antigen. The composition of amended claim 20 requires a self-antigen.

Neither Lu nor Chabalgoity cure the deficiency of either Bachmann or Gizurarson because neither Lu nor Chabalgoity teaches or suggests the claimed composition comprising an attenuated bacterium microorganism consisting of one of a *Shigella* strain and a *Salmonella* strain transformed with a vector capable of expressing an isolated non-amyloidogenic mammalian prion protein (*i.e.*, self-antigen) to elicit a humoral immune response that is associated with a mucosal IgA response and any concomitant immunoglobulin counterpart in other bodily fluids when introduced to a mammalian mucosal immune system.

For at least the reasons set forth above, amended claims 20 and 28 and pending claim 22 are not obvious over Bachmann, Gizurarson, and Lu, and further in view of Chabalgoity. Reconsideration of amended claims 20 and 28 and pending claim 22 and withdrawal of the rejection of these claims under 35 U.S.C. § 103(a) is respectfully requested.

New claim 55 is not obvious over Bachmann, Gizurarson, and Lu, and further in view of Chabalgoity for the same reasons as discussed in the foregoing comments because claim 55 is similar in scope to amended claim 20. New claim 55 differs from amended claim 20 by specifying an isolated non-amyloidogenic noninfectious mammalian prion protein. Thus, the arguments discussed in the foregoing comments with respect to claim 20 are also applicable to why new claim 55 is not obvious over Bachmann, Gizurarson, and Lu, and further in view of Chabalgoity.

* * * * *

Claims 23 and 46

The Examiner also has maintained her rejection claims 23 and 46 which indirectly depend from claim 20 under 35 U.S.C. § 103(a) as obvious over Bachmann, Gizurarson, and Lu and further in view of Benkirane for the reasons stated in the Office Action dated August 7, 2008. *See*, Office Action dated August 7, 2008, pages 12-13. According to the Examiner, it would have been obvious to provide a composition that induces immune responses wherein the antigenic peptides are composed of D-amino acids. *See*, Office Action dated August 7, 2008, page 12.

Claims 23 and 46 depend indirectly and directly, respectively, from amended claim 20, and each further specifies that the amino acid residues are D-amino acids. Thus, claims 23 and 46 are not obvious over Bachmann, Gizurarson, and Lu for the reasons discussed in the foregoing comments with respect to amended claim 20. Benkirane does not cure the deficiency of Bachmann, Gizurarson, or Lu because Benkirane does not teach or suggest the claimed composition comprising an attenuated bacterium microorganism consisting of one of a *Shigella* strain and a *Salmonella* strain transformed with a vector capable of expressing an isolated non-amyloidogenic mammalian prion protein to elicit a humoral immune response that is associated with a mucosal IgA response and any concomitant immunoglobulin counterpart in other bodily fluids when introduced to a mammalian mucosal immune system.

Based upon the foregoing comments, claims 23 and 46 are not obvious over the cited prior art. Reconsideration of pending claims 23 and 46 and withdrawal of the rejection of these claims under 35 U.S.C. § 103(a) is respectfully requested.

* * * * *

Claim 3

Claim 3 has been newly rejected under 35 U.S.C. § 103(a) as obvious over Bachmann and Gizurarson and further in view of Peretz (*Nature*, 2001, Vol. 412, p.739-743; hereafter "Peretz") and Kaneko et al. (*J. Mol. Biol.*, 2000, Vol. 295, p. 997-1007; hereafter "Kaneko"). The Examiner relies upon Bachmann and Gizurarson for the reasons as discussed in the foregoing comments with respect to claim 1. According to the Examiner, Peretz teaches that the region spanning amino acids 135-156 of an isolated prion protein is a critical determinant for inhibition of prion propagation by antibodies binding those particular amino acids. The Examiner states that Kaneko teaches that residues 90-144 of human prion protein are important for initiating prion disease. *See*, Kaneko, page 998 and Table 1 (page 1001). This rejection is respectfully traversed.

Claim 3 directly depends from claim 1, and further specifies amino acid sequences for the prion protein. Claim 3 is not obvious over Bachmann and Gizurarson for at least the reasons

discussed in the foregoing comments with respect to claim 1. Neither Peretz nor Kaneko cure the deficiency of either Bachmann or Gizurarson because neither Peretz nor Kaneko teaches or suggests the claimed composition consisting essentially of an isolated non-amyloidogenic mammalian prion protein (*i.e.*, a self-antigen) and an adjuvant to elicit a humoral immune response that is associated with a mucosal IgA response and any concomitant immunoglobulin counterpart in other bodily fluids when introduced to a mammalian mucosal immune system with a composition containing a self-antigen.

* * * * *

Claim 45

Claim 45 has been newly rejected under 35 U.S.C. § 103(a) as obvious over Bachmann, Gizurarson, Lu, and Chabalgoity, and further in view of Peretz. This rejection is respectfully traversed.

Claim 45 depends from claim 20, and further specifies particular amino acid sequences for the non-amyloidogenic prion protein. Claim 45 is not obvious over Bachmann, Gizurarson, Lu, and Chabalgoity for at least the reasons discussed in the foregoing comments with respect to claim 20. Peretz does not cure the deficiency of Bachmann, Gizurarson, Lu, and Chabalgoity because Peretz does not teach or suggest the claimed composition comprising an attenuated bacterium microorganism consisting of one of a *Shigella* strain and a *Salmonella* strain transformed with a vector capable of expressing an isolated non-amyloidogenic mammalian prion protein to elicit a humoral immune response that is associated with a mucosal IgA response and any concomitant immunoglobulin counterpart in other bodily fluids when introduced to a mammalian mucosal immune system.

* * * * *

For at least the reasons set forth in the foregoing comments, amended claims 1, 4, 9, 10, 20, 22, 23, 28, and 46 and new claims 54 and 55 are not obvious over the cited prior art.

Accordingly, it is respectfully requested that the Examiner reconsider and withdraw these rejections.

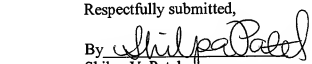
CONCLUSION

In view of the above remarks, it is respectfully submitted that the claims are in condition for allowance and such action is earnestly solicited.

If there are any other issues remaining which the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

Dated: June 30, 2009

Respectfully submitted,

By 

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